Case Study: Spindle Assembly Checkpoint

The spindle assembly checkpoint (SAC) prevents cell cycle progression until all chromo-somes are attached to the mitotic spindle. Defects lead to cell death, aneuploidy, ageing, and cancer.

Given a network model of SAC (below), we used artificial evolution to fix reactions improving checkpoint performance, hinting at further biological mechanisms to be explored in experiments. Shown on the right are the four modes of behaviour of the model: in phase IV the concentration of APCcd20 is supposed to rise. The improved model (red) outperforms the given model (blue).

References


Evolution of SBML Models

We have developed a software tool that can evolve - i.e. automatically design - SBML models fulfilling desired properties. Our algorithm involves two levels of evolution: a graph-based variant of Genetic Programming for structural modification of the reaction network and an Evolution Strategy for parameter fitting. The software is available upon request.

Summarizing Artificial Evolution

Utilizing the software, we successfully evolved a network that computes a square root. Shown here is the evolved network, together with its input-output behaviour.

Investigating Artificial Evolution

Benefits of the designed two-level approach are evaluated. We compared the effect of separating the evolutionary process into two levels with the effect of either a larger population or a longer run. The two-level approach significantly increases the evolutionary success.

Summary

Artificial evolution is a powerful tool to automatically devise complex systems capable of computational tasks. We have designed and implemented an algorithm for evolving biological models encoded in SBML. Analysing the evolutionary process, the results show that explicit distinction between structural modification of reaction network and parameter adjustment significantly increases the success rate of the evolution.

The software has also been used to modify a reaction network that computes a square root. Shown here is the evolved network, together with its input-output behaviour.

Hand-Crafted Reaction Network

A chemical reaction network is manually designed for a RS flip-flop with two NAND gates. Organization-oriented programming for a general chemical logic circuit is discussed in [3].

Recipe of chemical RS flip-flop

1. Each NAND gate is converted to 4 reactions.
2. Species representing contradictory situations are defined to decay: i = a, b, c, d: \( (s_i^0 + s_i^1 - \emptyset) \) (\( \emptyset \) empty set)
3. Operations are specified with inflows.

8 species and 12 reactions total